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## ORIGINAL ARTICLE

Assessment of levels of otoacoustic emission response in neonates with perinatal asphyxia<sup>☆</sup>

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## KEYWORDS

Asphyxia neonatorum;  
Apgar score;  
Neonatal screening

## Abstract

**Objective:** To evaluate the effects of perinatal asphyxia on the level of the response to transient otoacoustic emissions in infants.

**Methods:** Otoacoustic emissions in 154 neonates were performed: 54 infants who suffered asphyxia at birth, measured by Apgar score and medical diagnosis, and 100 infants without risk were compared. Scores less than 4 in the first minute and/or less than 6 in the fifth minute were considered as “low Apgar”. Statistical analysis of the data was performed using the Kruskal, Wilcoxon, and Mann-Whitney nonparametric tests.

**Results:** Lower levels of response were observed in transient otoacoustic emission in the group that suffered perinatal asphyxia, with significant values for the frequencies 2,000, 3,000, and 4,000 Hz in the right ear, and 2,000 and 4,000 Hz in the left ear.

**Conclusions:** The analysis of the intrinsic characteristics of the otoacoustic emissions evidenced low performance of outer hair cells in neonates who had perinatal asphyxia, which may affect the development of listening skills in this population.

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## PALAVRAS-CHAVE

Asfixia neonatal;  
Índice de Apgar;  
Triagem neonatal

## Avaliação dos níveis de resposta das emissões otoacústicas em neonatos com asfixia perinatal

## Resumo

**Objetivo:** Avaliar os efeitos da asfixia perinatal sobre os níveis de resposta das emissões otoacústicas por estímulo transiente em lactentes.

**Métodos:** Foi realizado, para comparação, o registro das emissões otoacústicas transientes em 154 neonatos: 54 bebês que sofreram asfixia perinatal, medida pela escala de

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Apgar e diagnóstico médico ao nascimento, e 100 bebês sem risco. Escores abaixo de 4 no primeiro minuto e/ou menores que 6 no quinto minuto foram considerados “Apgar baixo”. A análise estatística do conjunto de dados foi efetuada utilizando-se os testes não paramétricos de Kruskal, Wilcoxon e Mann-Whitney.

**Resultados:** Foram observados menores níveis de resposta nas emissões otoacústicas transientes para o grupo que sofreu asfixia perinatal, com valores estatisticamente significantes para as frequências de 2000, 3000 e 4000Hz na orelha direita e 2000 e 4000Hz na orelha esquerda.

**Conclusão:** A análise das características intrínsecas do exame de emissões otoacústicas transientes mostrou baixo desempenho das células ciliadas externas em neonatos que tiveram asfixia perinatal, o que pode afetar o desenvolvimento das habilidades auditivas nessa população.

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## Introduction

The Apgar score allows for the evaluation of newborn clinical status and identification of those in need of assistance, assessing the risks of perinatal asphyxia.<sup>1</sup> It consists of five criteria: heart rate, breathing effort, muscle tone, reflex irritability, and skin color. Each item is given values ranging from 0 to 2; the higher the score, the better the conditions at birth.<sup>2,3</sup>

This evaluation is performed by the neonatologist in the first, fifth, and tenth minute of life. However, perinatal asphyxia develops when there is significant tissue hypoperfusion and decreased oxygen supply, resulting from several etiologies in the peripartum period, which can cause neurological lesions and damage cochlear hair cells.<sup>2</sup> Apgar scores lower than 4 in the first minute and/or less than 6 in the fifth minute are considered risk factors for hearing loss and deserve attention.<sup>4</sup>

The first hearing assessment should be performed in the hospital nursery, using the otoacoustic emissions test for assessing the integrity of outer hair cells.<sup>5,6</sup> In most studies on hearing screening with otoacoustic emissions, the criterion used to characterize a normal exam is based on the presence of response.<sup>7</sup> However, for Aidan *et al.*,<sup>8</sup> one of the criteria to assess the actual status of the inner ear is the analysis of the intrinsic characteristics of this examination, such as the response magnitude of these emissions.

According to Basseto *et al.*,<sup>9</sup> full-term newborns have higher response amplitudes when compared to preterm newborns. The female gender and the right ear often have larger amplitudes.<sup>9,10</sup> The use of ototoxic drugs can cause lower amplitude response for otoacoustic emissions.<sup>11</sup>

From the perspective that analysis of the signal/noise ratio can provide additional information on the operation of outer hair cells, this study aimed to evaluate the levels of response to otoacoustic emissions evoked by transient stimuli in infants who had perinatal asphyxia.

## Methods

This study was approved by the Research Ethics Committee of Faculdade de Medicina de Botucatu (FMB) - Universidade

Estadual Paulista (UNESP), process No. 4156/2012. Data were collected at the Center for Rehabilitation of Hearing and Communication Disorders (Centro de Reabilitação dos Distúrbios da Audição e Comunicação - CERDAC), Hospital das Clínicas (HC) FMB-UNESP, from April 2012 to April 2013.

The study consisted of a non-concurrent cohort with a fixed population. Inclusion criteria were: a) having being born in the HC, b) presence of response in the otoacoustic emissions test, c) informed consent signed by the parents/guardians of the neonate. The exclusion criteria were: a) middle ear disorders diagnosed by the otorhinolaryngologist, b) presence of genetic syndromes, c) history of congenital infections, and d) use of ototoxic drugs.

For exposed individuals, an Apgar score of less than 4 in the first minute and/or less than 6 in the fifth minute was considered, as they are at risk for hearing loss, and this score was deemed “low Apgar”. The medical diagnosis of perinatal asphyxia for this group was also taken into account. The diagnosis of perinatal asphyxia was considered by the physician according to the clinical manifestations of the newborn, and was classified as neurological, cardiovascular, respiratory, metabolic, renal, gastrointestinal, or hematological. For those not exposed, only neonates with Apgar scores >7 in the first minute were selected for comparison.

There was no criterion for sample pairing, but potential confounders, gestational age, birth weight, and gender were tested (Tables 2, 3, and 4, respectively). As there was no evidence of significant probable associations with the outcome, the association between asphyxia and responses to otoacoustic emissions was analyzed without the need for correction.

Regarding the sample size calculation, since this was a non-concurrent cohort with a fixed population, no sampling dimension was required in the planning phase, but an estimate of test power, which ranged from 60% to 85%, depending on the frequency/ear. The power estimates considered a simple random sample, normality of outcomes, type I error of 0.05, and equal standard deviation between individuals with and without low Apgar.

The assessment of transient otoacoustic emissions was performed by a speech therapist specialized in audiol-

ogy. Responses from both ears were recorded, with the infant in a state of post-prandial natural sleep, in their mothers' arms, after 48 hours of life, in a silent room. If the infant awoke during the examination, the mother or guardian was advised to make the infant sleep again. The equipment used in all assessments was OtoRead/Interacoustics (Interacoustics do Brasil, RJ, Brazil), which allows for the recording of responses by introducing a probe, coupled with a microphone, in the ear canal.

The parameter PASS/FAIL was used as a criterion of analysis, described in the equipment protocol, with click stimuli, at an intensity of 83 dB peSPL, and six bands of frequencies (from 1,500Hz to 4,000Hz) were evaluated. Values that were considered PASS were emissions present in a signal/noise ratio of 6 dB in at least three consecutive frequency bands, including the 4,000 Hz band. The examination lasted 64 seconds, at most.

The signal/noise ratios considered for the analysis were frequencies 2,000; 3,000 and 4,000 Hz in both ears.<sup>12</sup> The values obtained at each frequency were compared between groups. Statistical analysis of the data set was performed using the nonparametric Kruskal-Wallis test, Spearman's correlation, and the Mann-Whitney test. The nonparametric test was used because the probabilistic distribution of the outcome was not identified. The descriptive level was highlighted in all tests and a significance level of 0.05 (5%) was used to reject the null hypothesis.

## Results

The study included 154 infants; sample characterization regarding gender, mean gestational age, and birth weight is shown in Table 1.

Before the analysis of perinatal asphyxia effect on the response level of otoacoustic emissions, the effect of gestational age and birth weight as potential confounders was investigated, but no statistical significance was observed (Tables 2 and 3).

However, when investigating gender, higher response amplitudes were observed for females at 2,000Hz, 3,000Hz, and 4,000Hz in the right ear, and 3,000Hz in the left ear (Table 4).

When comparing infants who suffered perinatal asphyxia with those who were healthy, lower response amplitudes were observed in individuals exposed to the risk indicator for hearing loss in all frequencies, except at 3,000Hz in the left ear (Table 5). In this case, the analysis was adjusted in relation to gender, as it was a potential confounding factor.

## Discussion

One of the current methods to diagnose early hearing loss is hearing screening by otoacoustic emissions, which aims at identifying infants with possible hearing impairment. Its analysis is based on the categorization of responses as present or absent,<sup>13</sup> but only those considered absent are candidates for diagnostic hearing evaluation by other methods, except in cases with suspected auditory neuropathy.

**Table 1** Sample characterization

Variable	n (%)
Female	93 (60.4%)
Male	61 (39.8%)
GA (weeks) <sup>a</sup>	39 (37-41)
BW (grams) <sup>a</sup>	3.281 (2.170-4.610)

<sup>a</sup> Summary in median, minimum, and maximum; GA, gestational age; BW, birth weight

In the study of the amplitude of otoacoustic emissions in relation to gender, significantly higher mean amplitudes were observed in newborn females, with a predominance of the right ear, as reported by other studies.<sup>8,14</sup> According to Cassidy & Ditty,<sup>14</sup> higher amplitudes in the examination of transient otoacoustic emissions in females when compared to males can be attributed to increased sensitivity of the outer hair cells in females. The analysis of the signal/noise ratio was also studied by other authors, such as Jiang *et al*,<sup>15</sup> who observed significantly lower amplitudes at frequencies of 1 kHz and 10 kHz in otoacoustic emission testing by distortion products in neonates with low Apgar scores, suggesting cochlear impairment, even with the presence of response. The magnitude of the response was also shown to be influenced by other risk factors, such as hyperbilirubinemia, prematurity, and exposure to ototoxic drugs.<sup>16-18</sup>

These findings demonstrate that it is necessary to better investigate the criteria of normal cochlear function, especially the pass/fail criterion of emissions, as studies in adult individuals have shown loss of cochlear function in those exposed to noise and ototoxic medication<sup>19-21</sup> long before the decrease in psychoacoustic thresholds, a factor that is not possible to investigate in the neonatal stage.

Literature shows that perinatal asphyxia is a major cause of failure in the neonatal hearing screening examination.<sup>22,23</sup> However, when analyzing the amplitude of otoacoustic emissions, this study observed lower values than those found in newborns with no risk indicators for hearing loss at birth. This indicates the possibility of damage to cochlear cells caused by tissue hypoxia, an information not taken into account for the criteria of normal otoacoustic emissions. Therefore, these infants should undergo clinical follow-up, as proper development of auditory skills depends on the integrity of the peripheral auditory system, and thus, parents should be informed. It is believed that other tests, such as brainstem auditory evoked potentials (BAEPs), already used in the clinical routine in neonates with low Apgar scores and electrocochleography, could assist in interpreting these findings.

It can be concluded that the analysis of the intrinsic characteristics of the transient evoked otoacoustic emission test showed lower amplitude values, suggesting lower performance of outer hair cells in neonates who suffered perinatal asphyxia at the frequency bands of 2,000, 3,000, and 4,000 Hz for the right ear, and 2,000 and 4,000 Hz for the left ear. Newborns that suffered asphyxia require clinical monitoring and electrophysiological and electroacoustic assessment to identify possible damage to the cochlea and auditory nerve cells, as well as to the development of auditory processing.

**Table 2** Association between gestational age and amplitude per frequency

	37 weeks			38 weeks			39 weeks			40 weeks			41 weeks			<i>p</i>
	med	min	max	med	min	max	med	min	max	med	min	max	med	min	max	
AMP_2,000Hz_RE	13	6	28	12	5	24	11	6	29	14	6	29	11	6	24	0.764
AMP_3,000Hz_RE	15	6	23	15	6	26	15	6	30	16	6	29	17	6	21	0.933
AMP_4,000Hz_RE	14	6	26	14	7	26	15	6	27	15	6	29	14	6	27	0.986
AMP_2,000Hz_LE	11	6	28	10	6	24	15	6	28	14	6	28	11.5	6	29	0.337
AMP_3,000Hz_LE	16	7	20	14	6	27	15	6	26	12	6	35	13.5	6	30	0.847
AMP_4,000Hz_LE	13	6	29	13	7	26	17	6	31	15	6	27	14	7	30	0.289

(\*) Kruskal Wallis; AMP, amplitude; RE, right ear; LE, left ear

Summary in median (med), minimum (min), and maximum (max)

**Table 3** Association between birth weight (BW) and amplitude of transient otoacoustic emissions

		AMP 2,000Hz-RE	AMP 3,000Hz-OD	AMP 4,000Hz-OD	AMP 2,000Hz-OE	AMP 3,000Hz-OE	AMP 4,000Hz-OE
BW	<i>r</i>	0.04	0.15	0.05	0.10	0.04	0.02
	<i>p</i>	0.633	0.068	0.557	0.209	0.641	0.810
	<i>n</i>	154	154	154	154	154	154

(\*) Spearman's correlation

BW, birth weight; AMP, amplitude; RE, right ear; LE, left ear; *n*, number of participants.

**Table 4** Association between gender and amplitude

	Female			Male			<i>p</i>
	Median	Minimum	Maximum	Median	Minimum	Maximum	
AMP_2,000Hz_RE	14	6	29	11	5	28	0.012 <sup>a</sup>
AMP_3,000Hz_RE	17	6	30	14	6	26	0.000 <sup>a</sup>
AMP_4,000Hz_RE	17	7	29	14	6	26	0.000 <sup>a</sup>
AMP_2,000Hz_LE	14	6	29	11	6	25	0.054
AMP_3,000Hz_LE	15	6	30	12	6	35	0.041 <sup>a</sup>
AMP_4,000Hz_LE	15	6	30	14	6	31	0.167

<sup>a</sup>≤0.05 Mann-Whitney test

AMP, amplitude; RE, right ear; LE, left ear.

**Table 5** Comparison between newborns with and without perinatal asphyxia (in relation to amplitude of response)

	Without perinatal asphyxia (100)			With perinatal asphyxia (54)			<i>p</i>
	median	minimum	maximum	median	minimum	maximum	
AMP_2,000Hz_RE	14	5	29	11	6	24	0.007 <sup>a</sup>
AMP_3,000Hz_RE	16	6	30	14	6	26	0.009 <sup>a</sup>
AMP_4,000Hz_RE	15	6	29	12	6	27	0.010 <sup>a</sup>
AMP_2,000Hz_LE	14	6	29	10.5	6	25	0.017 <sup>a</sup>
AMP_3,000Hz_LE	14	6	35	11.5	6	27	0.087
AMP_4,000Hz_LE	15.5	6	31	13	6	30	0.039 <sup>a</sup>

<sup>a</sup>≤0.05 Mann-Whitney test

AMP, amplitude; RE, right ear; LE, left ear.

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## Conflicts of interest

The authors declare to have no conflicts of interest.

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